

## CLAIMS

We claim:

1. A non-naturally occurring variant TNF- $\alpha$  protein comprising an amino acid sequence that has at least one amino acid substitution as compared to the wild-type TNF- $\alpha$  sequence, wherein said variant TNF- $\alpha$  protein will  
5 preferentially interact with the wild-type TNF- $\alpha$  to form mixed trimers incapable of activating receptor signaling.
2. A non-naturally occurring TNF- $\alpha$  protein according to claim 1 wherein said TNF- $\alpha$  protein has from 3 to 5 amino acid substitutions as compared to wild-type TNF- $\alpha$  sequence.
4. The non-naturally occurring TNF- $\alpha$  protein according to claim 1, wherein said substitutions are selected  
10 from the group of substitutions consisting of K112D, Y115T, D143K, D143R AND Y115I.
5. A recombinant nucleic acid encoding the non-naturally occurring TNF- $\alpha$  protein of claim 1.
6. An expression vector comprising the recombinant nucleic acid of claim 5.
7. A host cell comprising the recombinant nucleic acid of claim 5.
8. A host cell comprising the expression vector of claim 6.
9. A method of producing a non-naturally occurring TNF- $\alpha$  protein comprising culturing the host cell of claim  
15 7 under conditions suitable for expression of said nucleic acid.
10. The method according to claim 9 further comprising recovering said TNF- $\alpha$  protein.
11. A pharmaceutical composition comprising a non-naturally occurring TNF- $\alpha$  protein according to claim 1 and a pharmaceutical carrier.
12. A method for treating a TNF- $\alpha$  related disorder comprising administering a non-naturally occurring TNF- $\alpha$   
20 protein to a patient.
13. The method according to claim 12, wherein said condition is rheumatoid arthritis.